### OFFICE OF NAVAL RESEARCH

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Effective Smallpox Immunization of Young Adults

Ъу

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July 1976

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## EFFECTIVE SMALLPOX IMMUNIZATION OF YOUNG ADULTS

KENTUCKY UNIVERSITY

PREPARED FOR
OFFICE OF NAVAL RESEARCH

**JULY 1976** 

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Over the period October 1973 through June 1974, 10,257 Army recruits at Fort Knox, Kentucky were screened for smallpox vaccination reactions. 142 or 1.4% had a vesicular or pustular reaction at the vaccination site 7 days after routine intradermal jet injection of smallpox vaccine, denied prior vaccination and had no visible scar. 32 others with pustular reaction that had not begun to show any signs of drying by day 7, gave a history of prior vaccination and bore a vaccination scar. Thus a total of 17/(1.7%) were assentially non immune to introdermal inoculation of vaccinia virus. 335 control subjects were followed, 36% of whom presented major reactions, i.e., the presence of inducation and/or crythema on the 7th day surrounding a scab or drying pustule.

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Lymphadenitis, fever (temperature over .00°), chilis and fever, sore arm, axillary pain, sore throat, and general malaise occurred significantly more frequently among thom with a primary take than in the controls who experienced equivocal reactions. Lymphadenitis, axillary pain and core arm occurred significantly more frequently in those with a primary take than in the controls who experienced major reactions.

The primary vaccinated group had significantly more interference with their performance of duty than those with equivocal reactions. 20% visited sick call in contrast with only 3% of those with equivocal reactions.

Of those who denied previous vaccination and on whom no vaccination scar was noted 44% had hemaggiutination inhibition antibodies detectable at a 1:5 dilution, in contrast with 75% and 79% of the controls who developed major and equivocal react; as respectively.

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### ABSTRACT (continued)

A total of 78 newly hired employees of the University of Kentucky Hospital who denied receiving a smallpox vaccination within the past ten years were vaccinated by the Employee Health Service and monitored for virus shedding from the vaccination sites and throat.

A total of 231 throat swabs and 228 arm swabs were collected and tested on LLC-MK2 tissue cultures for the presence of vaccinia virus. None of the throat swabs were positive after ten days incubation of the inoculated tissue cultures. Eleven of the 44 skin swabs tested on days 2 and 3 were positive with a median viral plaque count of 32; 27 of 1 tested on days 4, 5 and 6 were positive, with a median plaque count of 42; 11 of 61 tested on day seven and over were positive, with a median plaque count of 3.

These low counts make the likelihood of viral contamination of a susceptible person remote and is consistent with the failure to find any instance in the literature of such cross infections in professional or casual contacts.

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### EFFECTIVE SMALLPOX INMUNIZATION OF YOUNG ADULTS

Abram S. Benenson and Irving A. Phillips University of Kentucky College of Medicine

ASSISTF® BY

M. Paul and S. Jenkins

WORK UNIT NO. NR 136-968

CONTRACT N00014-73-A-0385

### **OBJECTIVES**

(a) To define the adverse reactions associated with primary immunisation of young adults, their frequency and resulting morbidity,
(b) To develop effective immunizing techniques associated with minimal morbidity, and
(c) To develop diagnostic techniques permitting rapid recognition of smallpox.

### **ABSTRACT**

Over the period October 1973 through June 1974, 10,257 Army recruits at Fort Knox, Kentucky were screened for smallpox vaccination reactions. 142 or 1.4% had a vesicular or pustular reaction at the vaccination site 7 days after routine intradermal jet injection of smallpox vaccine, denied prior vaccination and had no visible sear. 32 others with pustular reaction that had not began to show any signs of drying by day 7, gave a history of prior vaccination and bore a vaccination scar. Thus a total of 174 (1.7%) were essentially non immune to intradermal inoculation of vaccinia virus. 335 control subjects were followed, 36% of whom precented major reactions, i.e., the presence of induration and/or erythema on the 7th day surrounding a scab or drying pustule.

Lymphadenitis, fever (temperature over 100°), chills and fever, sore arg, axillary pain, sore throat, and general malaise occurred significantly more frequently among those with a primary take than in the controls who experienced equivocal reactions. Lymphadenitis, axillary pain and sore arm occurred significantly more frequently in those with a primary take than in the controls who experienced major reactions.

The primary vaccinated group had significantly more interference with their performance of duty than those with equivocal reactions. 20% visited sick call in contrast with only 3% of those with equivocal reactions.

Of those who denied previous vaccination and on whom no vaccination scar was noted, 44% had hemagglutination inhibition antibodies detectable at a 1:5 dilution, in contrast with 75% and 79% of the controls who developed major and equivocal reactions respectively.

In this small series, no serious complications developed, consistent with an event occurring very rarely.

A total of 78 newly hired employees of the University of Kentucky Hospital who denied receiving a smallpox vaccination within the past ten

years were vaccinated by the Employee Health Service and monitored for virus shedding from the vaccination sites and throat.

A total of 231 throat swabs and 228 arm swabs were collected and tested on ILC-MK2 tissue cultures for the presence of vaccinia virus. None of the throat swabs were positive after ten days incubation of the inoculated tissue cultures. Eleven of the 44 skin swabs tested on days 2 and 3 were positive with a median viral plaque count of 32; 27 of 112 tested on days 4, 5 and 6 were positive, with a median plaque count of 22; 11 of 61 tested on day seven and over were positive, with a median plaque count of 3.

These low counts make the likelihood of viral contamination of a susceptible person remote and is consistent with the failure to find any instance in the literature of such cross infections in professional or casual contacts.

### REPORT ON THE NAVY PROJECT OF THE OFFICE OF NAVAL RESEARCH

### EFFECTIVE SMALLPOX IMMUNIZATION OF YOUNG ADULTS

The success of the WHO organized Smallpox Eradication Program logically has been followed by the cessation of routine vaccination against smallpox in the developed countries. Smallpox vaccination of U.S. citizens is now carried out only on those who have occasion to travel to areas where smallpox persists (only in Ethiopa at present, with a decreasing number of cases reported week by week) or those who are involved in laboratory studies in which they may have contact with variola virus. Within twenty years, it can be anticipated that the military recruit will enter service without prior vaccination.

One of the factors motivating the cessation of routine smallpox vaccination has been the reported frequency of significant adverse reactions among infants. However, many reports are present in the literature indicating that significant reactions, specifically post vaccinal encephalitis, occur more frequently in those who are vaccinated during or after adolescence. The serious complication of progressive vaccinia occurs in those with impaired cell-mediated immunity, such as occurs in leukemia or under immunosuppression.

This study was undertaken to obtain factual information on the cost, in terms of morbidity and time lost, of primary vaccination of the military recruit, and the risk to an immunosuppressed patient of exposure to a recently vaccinated individual. It was carried out in two parts.

### A. VACCINE REACTION STUDY AMONG MILITARY PERSONNEL

In order to define the reaction pattern experience by recruits who received primary vaccination, a project was set up at Ft. Knox, Kentucky with the collaboration of Colonel Chester Hanson, M.C., the post Preventive Medicine Officer. Recruits reporting to Ft. Knox are given basic immunization with tetauus-diptheria toxoids and poliomyelitis, meningitis, and monovalent influenza vaccines. 8 to 14 days later they received a dose of typhoid vaccine and smallpox vaccine by jet injection. A week later the smallpox vaccination reactions were read, and a dose of bivalent influenza vaccine administered. It was decided to utilize this routine immunization program, to define the morbidity resulting from primary vaccinations.

### Materials and Methods

All recruits were screened by one employee of the post Preventive Medicine Offer (Mr. S. Miller) one week (6 to 8 days) after the routine smallpox vaccination had been performed and those recruits who presented a vesicular or early pustular reaction were entered into the study. As controls for intercurrent illness or reaction to the influenza vaccine or intercurrent illness, the next two men in line were entered into the study. If one of these had a vesicular pustular reaction, he became an index case and additional men enrolled to maintain the one subject: two control ratio. Each man was seen daily and any signs of symptoms were recorded on the study form (appendix A). Surveillance was continued on the index case and his controls until three days after the erythema in the index case was clearly diminishing in size or the tamperature had returned to normal.

### Serological Studies

All recruits at Fort Knox were routinely bled into EDTA tubes for blood typing. These tubes were held on the clot by the blood bank until the study individuals had been identified, bloods were then provided to serve as the base line sera for the study. Follow-up bloods were drawn 14 and 28 days after the original smallpox vaccination. Hemagglutination inhibition tests were carried out by the method described by Hierholzer, et. al. (Applied Microbiology 18:816-832, 1969), using vaccinia hemagglutinable chicken cells. Meutralizing antibodies were carried out by the technique described by Wulff, et. al., (American Journal of Epidemiology 90:312-318, 1969) determining the serum dilution required to produce 50% plaque reduction on LLC-MK2 tissue culture—after 24 hour serum virus reaction times at 37°C.

### Analysis

Data were entered on McBee cards for scatistical analysis.

### Results

Over the period October 5, 1973 through July 12, 1974, 10,257 recruits with accessed, of whom 142 or 1.4% had a vesicular or pustular reaction at the accination site 7 days after routine intradernal jet injection of small-pox vaccine, denied prior vaccination and had no visible scar. 32 others with pustular reactions that had not begun to show any sign of drying by 7 days gave a history of prior vaccination and bore a scar of prior vaccination. Thus a total of 174 (1.7%) were essentially nonimmune to intradermal inoculation of vaccinia virus. 335 controls were followed, 36% of whom presented major reactions, i.e., the presence of induration and/or erythema on the 7th day surrounding a scab or drying pustule.

When the signs and symptoms occurring among those with a primary take are compared to the controls who experienced equivocal reactions, lymphadenitis, fever (temperature over 100°), chills and fever, sore arm, axiliary pain, sore throat, and general malaise occurred significantly more frequently; when compared with the controls who experienced major reactions, lymphadenitis, axillary pain and sore arm occurred significantly more frequently. Of interest was the greater frequency of reported sore throat among both the primary reactors and the control with major reactions than among the controls of an equivocal reaction; the likelihood that these differences occurring by chance is less than .01 in both cases. Over 90% of those with primary takes had one or more complaints or findings, in contrast to slightly over 1/3 of the equivocal reactors.

The primarily vaccinated group had significantly more interference with their performance of duty (Table 2) than those with equivocal reactions. 20% visited the sick call in contrast with only 3% of the equivocal reactors.

Planned serological studies have not been completed because of inconsistency in the results obtained with the neutralization test in use; this had been selected because it had been used in the NIH collaborative studies. Hemagglutination—inhibiting antibodies have been completed. Of those who denied previous vaccination and on whom no vaccination scar was noted, 44% had antibodies detectable at a 1:5 serum dilution, in contrast with 75% and 79% of the controls who developed major and equivocal reactions respectively (Table 3). In response to vaccination the index cases with HAI levels below 1:10 showed good

titer rises; with progressively higher revaccination titers, less response to vaccination is seen (figure 1). The same phenomenon is evident among the controls who developed major or equivocal reactions (figures 2 and 3).

It is of interest that the index group with no previous vaccinations did not differ in symptoms associated with the vaccination reaction, except that those with antibodies complained more frequently of axillary pain; however, there was no difference in the occurrence of lymphadenitis (Table 4).

### Discussion

This study does indicate a potentially significant cost to the military program associated with primary vaccinations, with approximately 20 sick call visits and 10 hospital days per hundred trainees. In this small series, no serious complications developed, consistent with an event occurring very rarely.

The finding of antibodies in the large number of those with no previous vaccination history is contrary to general experience. Since these men exhibited morbidity patterns comparable to those without antibody (Table 4), one must question whether errors had occurred in the selection of bloods to serve as a base line after they had been held for two weeks or longer on the clot in the blood bank. The possibility of mislabelling cannot be excluded.

The neutralization test methodology continues to be explored with the hope that a consistent test will permit further evaluation of these sera.

Signs and Symptoms Following intradermal smallpox vaccination

	Index Subject	Index Subject	Control		Previously vaccinated
	Primary (1)	~	Major (3)	Equivocal (4)	(Col. 2 + 3 + 4)
Total Number	142	32	121	214	367
Ivmnhadenitis	34.5%	25.0%	13.2%***	2.3%****	7.9%****
Temp. over 100	5.6	1	8.0	1.0*	**8.0
Temp. over 101	0.7	1	ı	0.5	
Chills and fever	24.6	18.7	16.5	12.6**	14.4**
Namsea and/or vomiting	5.4	3.1	4.9	2.3	3.3
Sorto arti	61.3	46.9	27. 3****	6.1***	16.6***
Date inder are	35.2	34.4	14.9***	1.4***	8.7***
Sore throat	40.1	37,5	42.1	24.3**	31.3
General melaise	18,3	6.2	12.4	7.5**	0°0
			•		
	ć	71 0	43.6	35.5	0.84
A With I or more	0.10	ν ας - 1 ας - 1	, w	21.5	24.0
A Wien only 1	10.0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	15.7	9.3	12,3
4 m	13.4	25.0	7.4	1.9	N
7	11,3	6.3	9.9	1.9	3.8
. rv	11.3	3.1	3.3	6.0	1.9
٥	4.2		0.8	•	0.3
Total Complaints	332	RJ RJ	159	124	338
Mean Number	2.27	1.72	1.31	0,58	0.92

Table 2

Effect of Primary Vaccination on Performance of Duty

	Index Primary	Index Primary type with scar	Cor Major Reaction	Controls Equivocal Reaction	All with previous vaccinations
Total Number	142	32	121	214	367
Interfered with Duty Relieved from Some Duty Sick Call Visit Hospitalized	7.7 2.1 19.7 3.5	3.1 3.1 15.6 3.1	3.3 13.2. 1.6:	0.5*** - 3.3**** 2.8	1.6** 0.3 7.6****
Number Who Went on Sick Call Number with 1 visit Number with 2 visits Number with 4 visits Number with 5 visits Total visits Total visits	28 15 1 36 25.4	28.1	16 14,9 16,9	7 6 1 1 8****	28 24 3 35****
Number Hospitalized Total hospital days Mean hospital days Mean hospital days/100 vaccinees	5 26 5.2 5.2	1. 1. 1.	2 2**** 1 1.7	6 18** 3 8.4	9 21**** 2.3 12.8

Table 3

Distribution of Hemagglutination Inhibition Antibody Titers

HAI Titer		Ind				Contr	o <b>ls</b>	
	Without		With	Scar	Majo		Equivo	cal
	No.	7	No.		No.	<u>%</u>	No.	
A Blood								
<b>⋖</b> 5	62	55.9	12	54.5	22	24.7	32	20.5
5	9	8.1	5	22.7	11	12.4	25	16.0
10	12	10.8	3	13.6	21	23.6	43	27.6
20	18	16.2	1	4.5	22	24.7	32	20.5
40	9	8.1	1	4.5	1.2	13.5	18	11.5
80	1	0.9	_	-	1	1.1	6	3.8
160		_	-	-	_		_	3.0
320	-	_	-	-	_	_	•	_
Geometric Mean	3.3		2.7		7.6		8.2	_
B Blood								
€5	_		_					
	5	3.65	1	3.1	-	-	6	2.9
5 10	6	4.38	2	6.3	2	1.7	12	5.7
20	29	21.7	<b>-</b>	-	25	20.7	49	23.4
20 '0	31	22.6	10	31.3	45	37.2	89	42.6
80	38	27.7	9	28.1	36	29.8	46	22.0
160	25	18.2	8	25.0	10	8.7	6	2.9
320	2	1.5	2	6.3	2	1.7	1	0.5
	1	0.7	-	-	1	-	-	_
Geometric Mean	23.9		32.7		24.7		17.6	
C Blood								
₹5	2	1.4			_		_	
5	2	1.4	•	-	1	0.8	9	4.3
10	12	8.5	1	3.2	5	4,2	11	5.3
20	26			-	31	26.3	58	27.9
40	26 57	18.4	7	22.6	35	29.7	94	45.2
80	37 32	40.4	12	38.7	30	25.4	33	15.9
160		22.7	8	25.8	15	12.7	1	0.5
320	10	7.1	2	6.5	1	0.8	-	-
Geometric Mean		-	1	3.2	-	-	-	-
Seometric Mean	37.2		44.7		22.2		15.1	

Table 4

Signs and Symptoms Among Index Cases
With and Without Preexisting HAI Antibodies

Signs and Symptoms	Group I HA	I Day Zero	Group IA HAI Day Zero					
		5	>	5				
	62	(%)	49	(%)				
Chills	19	(30.6)	12	(24.5)				
Nausea and Vomiting	3	(4.8)	4	(8.2)				
Sore Arms	32	(51.6)	<b>3</b> 5	(71.4)				
Pain under Arms	16	(25.8)	24	(49.0)*				
Sore Throat	25	(40.3)	27	(55.1)				
Ceneral Malaise	12	(19.3)	12	(24.5)				
Lymphadenitis	20	(32.2)	16	(32.6)				
Temperature 100° - 100.9°	2	(3.2)	0	-				
Temperature 101° - 102.9°	1	(1.6)	Ö	-				
Temperature > 103°	0	-	0	_				
Number of Subjects Whose Symptoms								
Interfered with Duty	2	(3.2)	5	(10.2)				
Number Relieved from Duty	0	`-	2	(4.1)				
Number Visited Sick Call	12	(19.3)	10	(20.4)				
Number Hospitalized	2	(3.2)	2	(4.1)				

<sup>\*</sup> p - <.05

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FIGURE 1

INDEX CASES

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# HEMAGGLUTINATION-INHIBITION TITERS

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HEMAGGLUTINATION-INHIBITION TITES

## HEMAGELTINATOR SERVEN TEST

	FIGURE 3
CONTR	OL-EQUIVOCAL REACTORS
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### B. VIRAL SHEDDING AND REACTION AMONG HOSPITAL EMPLOYEES

Concern has developed among the civilian population not only of the reactions produced in the vaccinee, but of the danger the vaccinee presented to others. The problem of eczema vaccination is well known; with the advent of immunosuppressive therapy, concern has risen that a continued vaccination program would jeopardize the welfare of transplant recipients, etc. This phase of the study was carried out to assess this risk, as well as to assess the reaction pattern among hospital employees.

### Materials and Methods

Newly hired employees of the University of Kentucky Hospital were routinely vaccinated against smallpox. Those who had not been vaccinated within 10 years were invited to participate in this project. Vaccination was carried out with Wyeth Dryvax vaccine using multiple puncture (15 punctures) with a bifurcated needle. After the punctures were completed, the vaccination site was wiped with a dry cotton ball to remove any excess vaccine. Those who volunteered were followed by the project nurse.

Symptoms were noted and a daily throat swab and a swab of the vaccination site were taken beginning on the second day after vaccination and continuing until the lesion was relearly subsiding. The skin swab was obtained with a dry sterile cotton swab with moderate pressure covering an area of about 2 centimeters, swabbing in a circle from the outside into the center. The cotton tip of the applicator was immediately broken off into a screw cap vial containing 3 ml of MEM(Eagle's) containing 0.5% bevine plasma albumin and 200 units/micrograms penicillin and streptomycin respectively per ml. If not tested immediately, the vials were stored at -70°C. At the time of inoculation all frozen specimens were quick thawed at 37°C and treated in the same manner as the direct inoculations.

For virus isolution, 1 ml of the fluid was inoculated onto the surface of each of 2 sheets of LLC-MK<sub>2</sub> cells grown in 2 ounce prescription bottles. After 48 hours incubation at 37°C one bottle was stained with crystal violet and plaques counted. The second bottle was similarly examined after 7-10 days incubation at 37°C.

### Results

A total of 78 individuals were studied under this program; all gave a history of prior vaccination. Forty developed major and 34 equivocal reactions; four were not seen during the 6-8 day post vaccination period and could not be classified. Among those with major reactions, 27.5% presented complaints during the period of observation, in contrast with only 5.9 of those with equivocal reactions, (Table I). These differences are statistically significant at the 0.05 level. When one looks at the individuals from whose skin surface virus was isolated it is evident that those with major reactions are much more likely to have free virus on the skin surface on serial swabbing (60.0 vs 14.7%), with a probability of this occurring by chance less than 0.0005. Among those with major reactions the presence of symptoms was not associated with a greater probability of virus recovery from the skin surface (symptomatic vs asymptomatic - chi squared, with Yates correction, 0.63). Virus was isolated from the arms of a total of 29 individuals (37.2% of the total); however, one patient refused symbling of her arm becurse she felt it was too tender - this was a puntular lesion which is expected to have been positive. This would give a total of 38% of the total

number on whose skin surface vaccinia virus was present at one time or another, with a total of 49 positive isolates obtained from 110 skin swabs taken from these individuals, for a percentage of 44.5%.

Of the total group, 228 skin swabs were collected for a total positivity of 21.5%. From the 231 throat swabs no virus was isolated; unfortunately none of these were primary vaccinations so that all subjects had a cellular immunity and presumably circulating antibodies. We were unable to obtain bleedings to answer this question.

Isolations were most frequent 4-8 days after vaccination; as would be anticipated, it was most frequently achieved from pustular lesions. However virus was recovered from simple papules, as late as the fifth day. On the second day, 32% still had virus on the skin surface. (Table II)

Analysis in terms of the type of reactions indicates that 29% of major reactions shed virus in contrast to 8% of those with equivocal reactions. (Table III)

Quantitative data were available on 217 virus isolation attempts. Counts over 200 per ml swab fluid were considered "too numerous to count"; of the 49 positive isolates, only 6 fell in this category; 9 were only positive after 7 days incubation. Eleven of 44 tested on days 2 and 3 were positive, with a median plaque count of 32; 27 of 112 tested on days 4, 5, and 6 were positive, with a median plaque count of 22; 11 of 61 tested on day seven and over were positive, with a median plaque count of 3.

### Discussion

These low counts make the likelihood that viral contamination of a susceptible person may occur remote. It is consistent with the failure to find any instance in the literature or from CDC of such cross infection in professional or casual contact. None of the throat cultures were positive even after 10 days of incubation (Table 2). In a previous series virus was recovered from the throat from 1 out of 82 cultures, (only 10 of these throat swabs were taken when the arm was positive). The one positive throat culture was taken on the fifth day after vaccinarion.

### **Acknowledgments**

We thank W. Fister, Dr. M. Benenson and R. Kinker for statistical assistance and M. Paul and S. Jenkins for technical assistance provided in these studies. Special appreciation is expressed to Colonel Chester Hanson, MC, US Army and Mr. Sam Miller of Fort Knox, Kentucky for their efforts in carrying out the field phase of this project.

TABLE I

### Symptom Complaints and Proportion of Subjects

### With Virus on Vaccination Site

### University Hospital Employees

Vaccination	Proportion with	Proportion with Virus Recovery from Skin									
Response	Symptoms	Symptomatic Subjects Asymptomatic All Subjects									
Major Reaction	11/40 27.5%	5/11 45.5% 19/29 65.5% 24/40 60%									
Equivocal Reaction	2/34 5.9%	0/2 - 5/32 15.62 5/34 14.74									
Not Classified	1/4	0/1 - 0/3 - 0/4 -									
Total	14/78 17.9%	5/14 35.7% 24/64 37 5% 29/78 37.2%									

### Major Reactors

- 1)\* Meadache; axillary pain, swelling day 7,8
- 2)\* "Sore arm" day 6,7
- 3)\* Malaise, sore arm, axillary pain day 6
- 4)\* Cervical adenitis day 5; some arm day 8
- 5)\* Temp 101° day 4
- 6) Refused awabbing too tender day 5,6,7
- 7) Nausea day 3
- 8) "Sore throat" day 4
- 9) Temp 101 day 4
- 10) Tender cervical nodes day 5,6
- 11) Axillary tenderness day 6-8

### Equivocal Reactors

- 1) Diarrhea and headache day 6
- 2) Sore throat day 6, "cold" day 7

### Not Classified

1) Cailed in as "sick" - day 5,6

<sup>\$ 5</sup>kin positive for vaccinia wires

TABLE II

Vaccinia Virus Isolations From Throat Swabs and Vaccination Sites

By Type of Lesion and Day After Vaccination

Ckin Lesion						Days	Afte	r Vacc	inatio	<u>n</u>				T	otal	
	2	3	4	5	6	7	8	9	10	11	12	13	14	Tested	Pos.	% Pos
Papule	25**	16 <sup>2</sup>	20 <sup>5</sup>	11 <sup>1</sup>	3	1	-	ALD		**	-	***	-	76	16	21.1%
Vesicle	11	5	9 <sup>2</sup>	113	4	1	-	•••	-	-	-	-	-	31	6	19.4%
Pustule	-	-	21	12 <sup>9</sup>	15 <sup>5</sup>	61	4,5	1	-	1	-	-	•••	41	18	43.9%
Dry, Pustul	e -	-	•	1	21	£ 1	61	11	_	-	-	-	**	18	4	22.2%
Scab c Ery.	_	-	2	2	8	10²	6 <sup>1</sup>	1	***	1	31	1	1	35	4	11.43
Scah	-	-	1	5	4	31	6	_		1	1	1	-	22	1	4.5%
Nothing	-	-	1	1	1	-	•	-	-	**	-	•	-	3		•
Total Cult. Pos. % Pos.	26 9 34.6	21 2 9.5	35 8 22.9	43 13 30.2	37 6 16.2	29 5 17.2	22 4 18.2	3 1 33.3	en en	3	4 1 25	2	1	226	49	21.7
Ar. Swabs	26	21	35	45	38	31	22	3	-	3	4	2	1	231	0	0;

<sup>\* 25</sup> sates cultured; 8 positive for vivus

TABLE III

Vaccinia Virus Isolativas From Vaccination Sites

By Type of Reaction

Skin Lesion						Days	After	Vace	inutio	<u>n_</u>				70	otal	
	2	3	4	5	6	7	.8	9	10	11	12	13	14	Tested	Pos.	Z Po
	<del></del>	····		+ <del></del>		Ŋ	lajor	React	ors	· · · · · · · · · · · · · · · · · · ·		****				
Papule	95*	61	105	2	•	1	-	-	***	**	-	•	-	28	11	39.
Vesicle	11	1	62	113	3	1	-	-	-	-	•	-	-	23	6	26.
Pustule	-	•	21	129	15 <sup>5</sup> ,	. 61	42	1	_	1	•	400	-	41	18	43.9
Dry, Pustule	-	-	•	1	21	81	61	11	-	_	-	-	-	18	4	22.
Scab & Ery.		-	1	1	7	92	61	1	<del>-</del>	1	31	1	1	31	4	12.
Scab	-		-	-	1	11	4	-	-	1	1	1		9	ŀ	11.3
Total Cult. Pos % Pos.	10 . 6 60.0	6 1 14.3	19 8 42.1	27 12 44.4	28 6 21.4	26 5 19.2	20 4 20.0	3 1 33.3	es 65	3 0 -	4 1 25	2 0	1 -	150	44	29.
·	•					E	uivoc	al Ro	actors	<b>.</b>				1		*
<b>Papule</b>	143	91	10	91	3	-	-	-	-	-	-	-		45	5	11.
Vesicle	-	4	2	-	-	-	-		-	_	-	-		6	0	
Sçab č Ery.	-	••	1	1	-	-	-	-	•			_	-	2	0	ryte.
Scab	-		1	5	3	1	-	-	_	_	_	-	-	10	0	••
Nothing	-	-	1	1	1		•	-	-	•		-	-	3	0	-
Total Cult. Pos % Pos.	14 . 3 21.4	13 1 7.7	15	16 1 6.3	7	1 -	40 40 40	-	***	-	••	-	-	66	5	7.
				•			Not (	Classi	fied					•		
Papule	2	1	-	-	-	-	-	-	-	•	-	-	-	3	-	
Vesicle .	-	-	1	-	1	-	-	-	••	-	-	-	-	2	-	
Scab & Ery.	_		-	-	1	1.	-	-	-	-	-	-	-	2	-	
Scab	-	**	-	•••	••	1	2	-	••	•-		-	-	3	•	
Total Cult. Pos	2	1 -	1	,	2	2	2	## ##		-	-	-	-	10	0	

<sup>\* 9</sup> sites cultured; 5 por inice for virus

Appendix .

ervice Numbers

Rostar Nuchers

Companys

Late of Vaccinations

こうちょうないことをなるというないというところなるというになっていると

Dete of Prior Veccinations

Sear of Provious Vaccination: No

>120

Describe Central

Reaction ass

Day After Vassination Diameter of Central Reaction (cm) Observations and Complaints: Area of Induration (cm.) Sere Arm (left or right) Contral Lesion Resetton Relieved from some Duty Hauses and for Vomiting free of Redness (on.) Not Relieved from but Cohort Roster Numbers Interfered with Duty No Effect on Buty Chills and Fever General Malaise Fain Under Arm Lymphadenitis Terrerature Sore Throat

-K-

1yphoid Influence

*T*c Polto

Rubella

Other

Actend

\*Other Vaccines

Ste Scab sins

S= Seab

Reariss D.P. Dried

Pape Fabile Fust Fustule

O= Nothing V= Vesicia

KI Titar

SN fiter

Study Number

\*To be completed by laboratory

Date of Additional Bloods

Date of Initial Bloods

other: (Describe)

Sick Call Visit

copitalized